Setting positive end-expiratory pressure in the severely obstructive patient

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Purpose of review
The response to positive end-expiratory pressure (PEEP) in patients with chronic obstructive pulmonary disease (COPD) requiring mechanical ventilation depends on the underlying pathophysiology. This review focuses on the pathophysiology of COPD, especially intrinsic PEEP (PEEPi) and its consequences, and the benefits of applying external PEEP during assisted ventilation when PEEPi is present.

Recent findings
The presence of expiratory airflow limitation and increased airway resistance promotes the development of dynamic hyperinflation in patients with COPD during acute respiratory failure. Dynamic hyperinflation and the associated development of PEEPi increases work of breathing and contributes to ineffective triggering of the ventilator. In the presence of airflow limitation, application of external PEEP during patient-triggered ventilation has been shown to reduce inspiratory effort, facilitate ventilatory triggering and enhance patient-ventilator interaction. To minimize the risk of hyperinflation, it is advisable to limit the level of external PEEP during assisted ventilation after optimization of ventilator settings to about 70% of the level of PEEPi (measured during passive ventilation).

Summary
In patients with COPD and dynamic hyperinflation receiving assisted mechanical ventilation, the application of low levels of external PEEP can minimize work of breathing, facilitate ventilator triggering and improve patient-ventilator interaction.

Keywords
chronic obstructive pulmonary disease, dynamic hyperinflation, external positive end-expiratory pressure, intrinsic positive end-expiratory pressure

INTRODUCTION

Exacerbations of chronic obstructive pulmonary disease (COPD) are one of the main indications for receiving mechanical ventilation worldwide [1,2]. Although mechanical ventilation is two to four times more likely to be initiated in patients with COPD than in patients with adult respiratory distress syndrome (ARDS) [1,2], most of the recent literature on the delivery of mechanical ventilation has focused primarily on ARDS and not COPD [3–5].

Positive end-expiratory pressure (PEEP) is an intervention that can be applied to all modes of mechanical ventilation. The response to PEEP in ventilated patients with COPD, however, depends on the underlying pathophysiology. This review focuses on the pathophysiology of airway obstruction in COPD, especially the development of dynamic hyperinflation and intrinsic PEEP (PEEPi), during acute respiratory failure. The benefits of adding external PEEP during assisted ventilation in the presence of PEEPi will also be discussed.

PATHOPHYSIOLOGY OF AIRFLOW OBSTRUCTION

Expiratory airflow limitation and dynamic hyperinflation

In stable patients with COPD, inspiratory flow resistance is approximately 6 $cmH_2O/l/s$ above normal [6]. During an episode of acute respiratory failure, resistance can increase by as much 13 $cmH_2O/l/s$ [7]. Expiratory resistance in markedly increased in patients with COPD [8]. In ventilated patients with

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KEY POINTS

- Dynamic hyperinflation and intrinsic PEEP (PEEPi) are commonly present in patients with COPD receiving mechanical ventilation.
- PEEPi increases work of breathing and contributes to ineffective triggering of the ventilator.
- The benefits of external PEEP in patients with COPD is dependent on the presence of airflow limitation and patient-triggered ventilation.
- External PEEP can be titrated to about 70% of static PEEPi with careful monitoring of plateau pressure during volume-cycled ventilation and tidal volume during pressure-cycled ventilation.

COPD, the ratio of expiratory to inspiratory flow resistance ranges from 3.8 at low lung volumes to 1.6 at high lung volumes [9,10].

The main problem in COPD is not only the increase in airway resistance *per se*, but also expiratory airflow limitation. Expiratory flow limitation refers to a condition in which expiratory flow cannot increase as a result of decreased tethering of the airways secondary to rupture of elastic fibers [10].

Expiratory airflow limitation occurs in about 60% of stable patients with COPD [11] and is universally present during episodes of acute respiratory failure [12].

The minimum time required to exhale from a given lung volume to relaxation volume of the respiratory system is determined by the maximum expiratory flow [10]. The amount of time taken by lung units to empty during exhalation, referred to as time constant of the respiratory system, is calculated as the product of compliance and resistance. One time constant indicates the time required to empty 63% of the volume inhaled and three time constants represents the time required to empty 95% of the volume inhaled. When the time for expiration is less than minimum time required for exhalation, inspiration will begin before the respiratory system has returned to its relaxation volume, a state known as dynamic hyperinflation. When patients with severe COPD and expiratory flow limitation develop tachypnea, they necessarily shorten the time available for expiration (expiratory time). The decrease in expiratory time means that the next inspiration will begin before the respiratory system has returned to its relaxation volume, thus producing dynamic hyperinflation. In addition to flow limitation, increased airway resistance also contributes to dynamic hyperinflation. Increased airway resistance will increase the time constant; the higher the time constant, the longer the time required to have complete exhalation. By prolonging the time constant of the respiratory system, increased resistance will decrease the time needed for expiration [13].

Intrinsic positive end-expiratory pressure

Dynamic hyperinflation is almost consistently associated with an increase in end-expiratory elastic recoil of the respiratory system. The positive recoil pressure is referred to as auto or PEEPi [14–16]. PEEPi can be quantified in relaxed patients (under passive conditions) using an end-expiratory hold maneuver on a mechanical ventilator immediately before the onset of the next breath (static PEEPi) [15,17,18]; end-expiratory occlusion allows measuring the pressure in the alveoli in the absence of complete airway collapse. PEEPi can also be quantified as a change in airway pressure needed to reduce expiratory flow to zero and initiate lung inflation by the ventilator (dynamic PEEPi) [19,20]. In patients with COPD, dynamic PEEPi is lower than static PEEPi; this discrepancy is attributed to the presence of time-constant inequalities within the lungs [21,22].

In patients with active inspiratory muscles, measurements of static PEEPi are not reliable because patients react unpredictably to end-expiratory occlusion [23,24] (Fig. 1). When muscles are actively contracting as during assisted ventilation, measurement of dynamic PEEPi requires the insertion of balloon-tipped esophageal catheter [25,26]. Dynamic PEEPi is measured as the amount of decrease in esophageal pressure from the onset of inspiratory effort to the start of inspiratory flow [10,25,27] (Fig. 2). This measurement of dynamic PEEPi has been used in acutely ill patients with COPD and is valid provided that the expiratory muscles are relaxed at end-expiration. When expiratory muscles are contracting, the pressure developed in the abdomen is transmitted through the relaxed diaphragm and raises intrathoracic pressure [27–29]. Accordingly, assessing PEEPi using esophageal pressure will overestimate the true end-expiratory elastic recoil pressure [28,29].

Consequences of intrinsic positive end-expiratory pressure

Increase in respiratory work and ineffective triggering

Dynamic hyperinflation and PEEPi has adverse effects on pulmonary mechanics and respiratory work. In ventilator-dependent patients with COPD, PEEPi accounted for as much as 40% of overall respiratory work [30,31]. In patients with COPD recovering from

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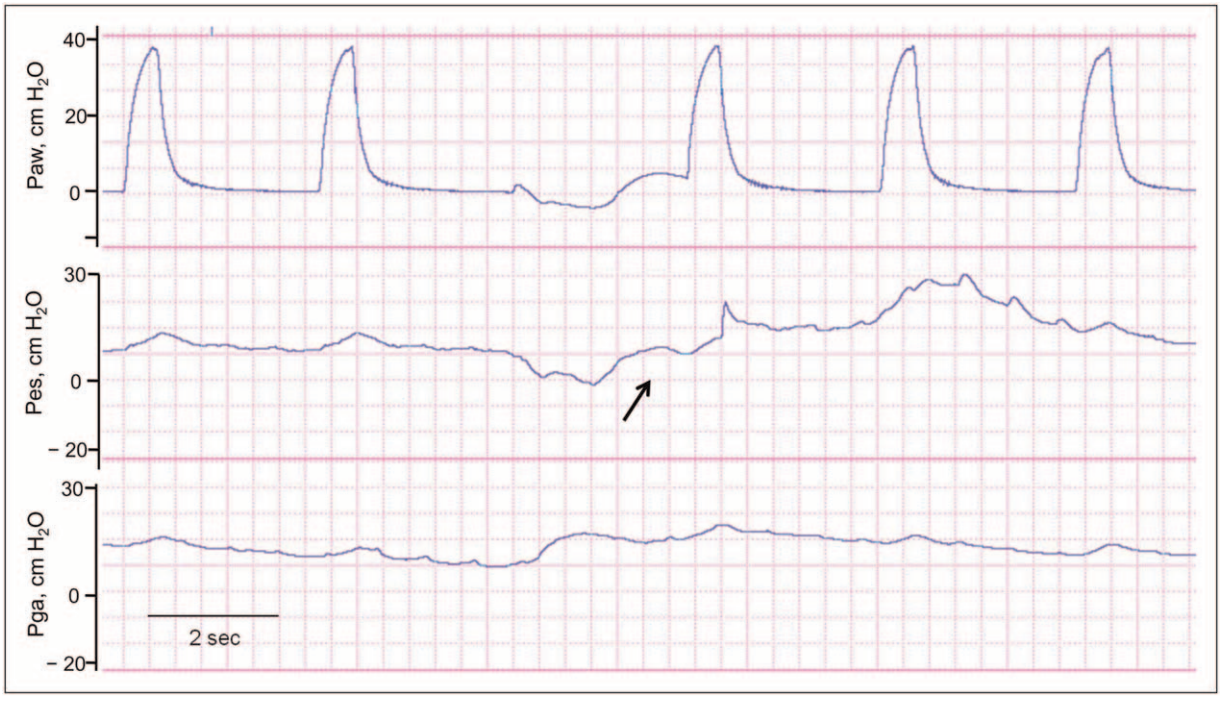

FIGURE 1. Airway pressure (Paw), esophageal pressure (Pes), and gastric pressure (Pga) in a patient with COPD during mechanical ventilation. The airway was occluded during expiration in order to quantify intrinsic PEEP (PEEPi). The patient made an expiratory effort during the occlusion (arrow). Reproduced from Jubran (Figure 48–14 of ref [24]).

an episode of respiratory failure necessitating mechanical ventilation, about 20–25% of the inspiratory muscle effort was required to overcome PEEPi during a T-piece weaning trial [7].

Hyperinflation increases work of breathing because inspiration occurs at the upper, less compliant portion of the pressure-volume curve of the lung, where inwardly directed elastic recoil of the chest wall poses an additional elastic load. The positive pressure in the alveolus at the end of expiration means that the patient has to first generate negative inspiratory pressure equal in magnitude to the opposing elastic recoil pressure (level of PEEPi) before inspiratory flow can be initiated, that is threshold inspiratory load [10]. If a patient with PEEPi is triggering a ventilator, he or she has to generate a negative pressure equal in magnitude to the level of PEEPi in addition to the set minimum circuit pressure drop before a ventilator-assisted breath is initiated. This is one factor that accounts for the common occurrence of failure to trigger the ventilator despite obvious respiratory effort [32] (Fig. 3).

In a study of factors contributing to ineffective triggering, a decrease in the magnitude of inspiratory effort at a given level of assistance was not the cause; indeed, effort was 38% higher during nontriggering attempts than during the triggering phase of attempts that successfully opened the ventilator valve [33]. Significant differences, however, were noted in the characteristics of the breaths before the triggering and nontriggering attempts. Breaths before nontriggering attempts had shorter respiratory cycle times and expiratory time and higher static PEEPi than did the breaths before triggered attempts. These findings suggest that ineffective triggering did not result from a decrease in the magnitude of effort, but rather from inspiratory efforts that were premature and insufficient to overcome the elevated elastic recoil pressure associated with dynamic hyperinflation [10,33].

In addition to an increase in elastic recoil, expiratory muscle activity can contribute to an elevated PEEPi [29,34–36]. In healthy individuals receiving pressure support ventilation in whom airflow limitation was induced with a Starling resistor [28], PEEPi was more than 30% higher at the start of nontriggering attempts than before triggering attempts, similar to the condition in critically ill patients [33]. Although the elastic recoil pressure (quantified as PEEPi minus increase in gastric pressure) was higher before nontriggered attempts than triggered attempts, the level of expiratory effort (quantified as the expiratory increase in gastric pressure), was similar before nontriggering and triggering attempts, indicating that expiratory effort did

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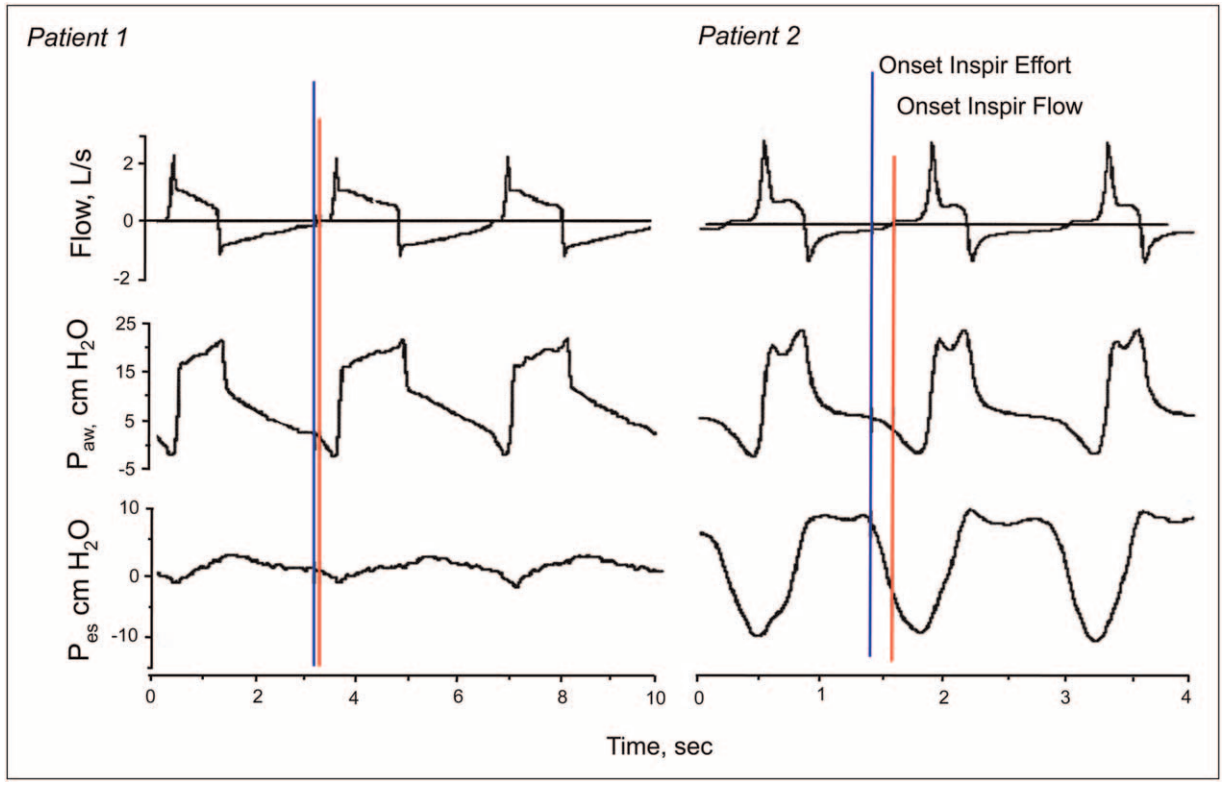

FIGURE 2. Flow, airway pressure (Paw), and esophageal pressure (Pes) in Patient 1 (left) and Patient 2 (right) with COPD receiving pressure support ventilation (no external PEEP is applied). Dynamic intrinsic PEEP, estimated as the difference in esophageal pressure between the onset of inspiratory effort and the onset of inspiratory flow was 0.5 cmH_2O in the patient on the left and 10.6 cmH_2O in the patient on the right. Reproduced from Tobin (Figure 4 of ref [10]).

not contribute to generation of PEEPi. Accordingly, it is the increase in elastic recoil and not expiratory effort, that is responsible for failure to trigger the ventilator.

Respiratory muscle dysfunction

Dynamic hyperinflation impairs respiratory muscle function by worsening the length-tension relationship of the muscles, decreasing the zone of apposition and the curvature of the diaphragm, and changing the mechanical arrangement of costal and crural components of the diaphragm [10].

Hemodynamic compromise

Alveolar overdistension and PEEPi can severely decrease cardiac output [15] by impeding venous return and increasing right-ventricular afterload [37,38].

Hemodynamic compromise as a result of PEEPi is more magnified in COPD because the abnormally compliant lungs transmit a high fraction of alveolar pressure to intrathoracic vessels [15]. During cardiopulmonary resuscitation, PEEPi in patients with airway obstruction may cause pulseless electrical activity [39,40].

Barotrauma

Application of external PEEP can lead to overdistension and rupture resulting in pneumomediastinum and pneumothorax [41] not only in COPD patients but in all ventilated patients. While the same complication may occur with increased levels of PEEPi, systematic studies have not been conducted on this matter.

Errors in monitoring

The presence of PEEPi can lead to erroneous measurements of static compliance of respiratory system, computed as tidal volume divided by plateau pressure minus set PEEP [18]. PEEPi commonly goes undetected, since it is not registered on the pressure manometer of the ventilator, which is open to the atmosphere. Accordingly, in the presence of PEEPi, the total PEEP may markedly exceed the set PEEP. Failure to take PEEPi into account caused a 48% underestimation in the static compliance [19].

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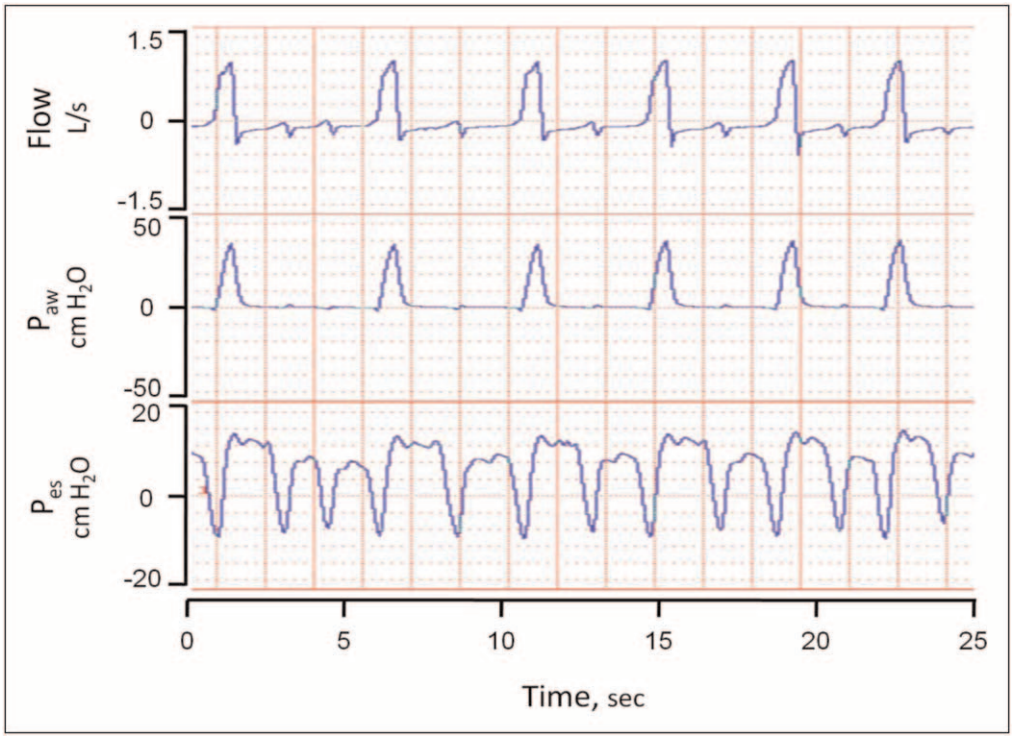

FIGURE 3. Flow, airway pressure (Paw), and esophageal pressure (Pes) in a patient with COPD who is receiving assist-control ventilation. The patient's intrinsic respiratory rate is 28 breaths per minute, whereas the number of breaths delivered by the ventilator is 16 breaths per minute. That is, 43% of the patient's inspiratory efforts fail to trigger ventilator assistance. Reproduced from Tobin (Figure 53–12 of ref [32]).

USE OF EXTERNAL POSITIVE END-EXPIRATORY PRESSURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

In patients with COPD receiving assisted mechanical ventilation, the primary goals of PEEP are to enhance triggering sensitivity, decrease work of breathing secondary to the inspiratory threshold load effect of PEEPi, and optimize patient-ventilator interaction.

An effective approach to reduce or eliminate PEEPi is to decrease minute ventilation even if this means development of alveolar hypoventilation – permissive hypercapnia [42]. In patients with COPD ventilated with assist-control ventilation, clinicians often increase inspiratory flow to decrease inspiratory time in the hope of allowing more time for expiration and thus decrease PEEPi. Because increases in flow commonly lead to an increase in respiratory rate [43], the anticipated reduction of expiratory time might increase PEEPi.

In patients with COPD while receiving assist-control ventilation, increase in flow from 30 to 90 l/min increased the respiratory rate but decreased PEEPi [44]. Decrease in PEEPi was the result of a paradoxical increase in expiratory time, which allowed more time for lung deflation. The investigators reasoned that the shortened inspiratory time combined with time-constant inhomogeneity of COPD caused over-inflation of some lung units to persist into neural exhalation. Continued inflation during neural exhalation causes stimulation of the vagus nerve, which prolongs expiratory time [44].

Physiological benefits of positive end-expiratory pressure

Addition of external PEEP can decrease work secondary to the inspiratory threshold load effect of PEEPi [9,30,45]. To start inspiratory flow, alveolar pressure must be lowered below ambient pressure. During normal spontaneous breathing, this is accomplished by only a small decrease in pleural pressure. For alveolar pressure to fall below ambient pressure in the presence of hyperinflation, however, a much greater decrease in pleural pressure is needed. If ambient pressure is elevated by the application of external PEEP, inspiration is more easily accomplished because alveolar pressure needs to be decreased only below the level of external PEEP (rather than below zero). This may seem paradoxical:

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external PEEP, which is commonly used to induce hyperinflation in patients with microatelectasis, is being used to decrease the work of breathing induced by hyperinflation [32].

This conundrum can be explained by the analogy of a waterfall [46]. The height of the waterfall represents the critical closing pressure of airways in patients with COPD and PEEPi. The driving pressure for flow throughout expiration is the level of PEEPi minus critical closing pressure. Elevating downstream pressure with external PEEP has no influence on either expiratory airflow or the pressure upstream (PEEPi) from the site of critical closure. This situation exists until downstream pressure is elevated to a value equal to the critical closing pressure. Once downstream pressure is elevated above the critical closing pressure (the height of the waterfall), however, the pressure upstream increases immediately, and hyperinflation is exacerbated [32,46].

The application of external PEEP decreases the work of inspiration in patients with PEEPi during patient-triggered ventilation and improves patient-ventilator interaction only in the setting of airflow limitation [9,10,47]. In patients without airflow limitation, the effective expiratory driving pressure is elastic recoil pressure minus the pressure at the airway opening. Accordingly, the application of external PEEP will decrease the expiratory driving pressure and produce a decrease in expiratory flow at all lung volumes and an increase in end-expiratory lung volume [47,48]. Adding extrinsic PEEP lower than PEEPi reduces the amount of work needed to trigger the ventilator even in the absence of airflow limitation (as long as airflow limitation means partial airway collapse).

Although external PEEP can help decrease inspiratory work, it does nothing to relieve the accompanying hyperinflation, which has other detrimental effects. It is important to keep in mind that patients with airflow limitation have heterogenous distribution of lung units, each with its own critical closing pressure. Because of the regional inhomogeneities among lung units, the average level of PEEPi must exceed the lowest regional alveolar pressure. Thus, external PEEP equal to PEEPi could cause hyperinflation in the faster-emptying lung units [49]. To minimize this risk, it is reasonable that after optimization of ventilator settings, to limit the level of external PEEP to about 70% of the level of PEEPi (measured using end-expiratory hold maneuver while patient is passively ventilated) [50]. Indeed, several studies have demonstrated that titration of PEEP to about two-third of the level of PEEPi reduced inspiratory effort and the number of ineffective efforts; it also facilitated ventilatory triggering by decreasing both inspiratory effort and delay

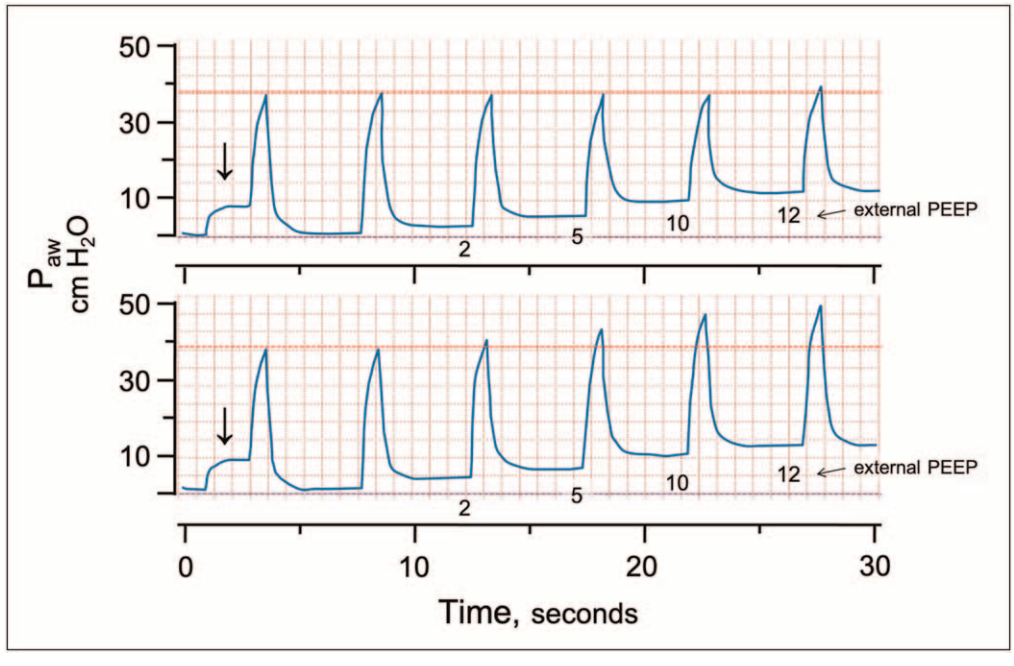

FIGURE 4. Airway pressure (Paw) versus time during controlled mechanical ventilation in a patient with expiratory flow limitation (upper) and in a patient without expiratory flow limitation (lower). In both patients, static intrinsic PEEP (PEEPi) (arrow) is 10 cmH_2O. In the presence of expiratory flow limitation upper), peak airway pressure increases only when external PEEP is 12 cmH_2O (dotted red line). In the absence of expiratory flow limitation (lower), application of external PEEP causes a proportional increase in peak airway pressure. Reproduced from Laghi (Figure 31–10 of ref [53]).

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between the onset of inspiratory effort and initiation of assistance [9,30,45,51].

Titration of external positive end-expiratory pressure

The beneficial effect of external PEEP in ventilated patients with COPD is dependent on the presence of airflow limitation and patient-triggered ventilation [37,52▪▪,53]. Because its unpredictably on hyperinflation, the titration of external PEEP should be guided by measurement of static PEEPi [37,54] performed during passive ventilation. When PEEPi is present, the rise in airway pressure during the occlusion maneuver at end-expiration should be maintained until a plateau is reached. In the presence of airflow limitation, titration of PEEP should continue until peak and plateau airway pressure show a sizeable increase (volume-cycled ventilation) or when tidal volume starts to decrease (pressure-cycled ventilation) [37,53] (Fig. 4).

CONCLUSION

In the past, PEEP was avoided in patients with COPD because of the fear of aggravating hyperinflation. Subsequent work indicates that the application of PEEP during assisted ventilation in patients with airflow limitation makes it easier for the patient to trigger the ventilator, thereby improving patient-ventilator synchrony and decreasing respiratory work. After optimization of ventilator settings, external PEEP can be titrated to about 70% of static PEEPi with careful monitoring of plateau pressure during volume-cycled ventilation and tidal volume during pressure-cycled ventilation.

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Conflicts of interest

A.J. has no conflict of interest.

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- ▪▪ of outstanding interest

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